REMARKS

Claims 1–27 are pending in the present application. Claims 11–17 and 19–25 have been cancelled. Claim 18 has been cancelled for the purpose of rewriting and has been represented as new claim 29. Claims 26 and 27 have been cancelled. Claims 1–10 have been amended and new claims 28 and 30–44 have been added. The amendments to the claims and new claims are supported throughout the specification and are not narrowing. The following addresses objections of the Examiner in terms of the points raised in the outstanding communication:

Election/Restriction

(1) Applicant acknowledges the Examiner's indication that restriction of the claims to group 1 (claims 1–10, 17, 18, 26 and 27) is final and the withdrawal of claims 11–16 and 19–25.

(2) The Examiner has indicated that claim 17 also should be restricted from the elected group 1. Applicant acknowledges the Examiner's withdrawal of claim 17 from the elected group of claims.

Priority

(3) Please find enclosed a Certified Copy of United Kingdom Patent Application No. 9801902.9 as filed on January 29, 1998. Please note that this Application was filed with the PCT authorities as the corresponding International Patent Application No. PCT/GB99/00309 on March 2, 1999 in accordance with PCT Rule 17.1(a) or (b). The priority document therefore should have been forwarded by request to the USPTO by the PCT authorities previously in accordance with PCT Rule 17.2(a).

Abstract

(4) In accordance with 37 CFR 1.72(b), please find enclosed the required Abstract of the disclosure on a separate sheet.

Specification

(5) Page 35 of the description has been amended wherein the embedded hyperlink and/or other form of browser-executable codes have been deleted.

(6) With regards to the Examiner's objection, pages 5 and 45 of the description have been amended wherein position marked "-463" has been replaced with "-436". The Examiner will note that this is a correction to an obvious error as, in view of Figure 4a, the position of the hProm505 construct should have read -436 to give rise to a 505 bp construct.

Claim Objections

(7) The Examiner has objected to claims 26 and 27 under 37 CFR § 1.75(c). The Examiner will note that Applicant has cancelled these claims.

Claim Rejections–"Use"

(8) The Examiner has rejected claim 18 under 35 U.S.C. § 112 as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention and under 35 U.S.C. § 101 as not to be a proper process claim. Applicant has rewritten this claim (new claim 29) to show that the method referred to for the treatment of cancer utilizes the vector prepared according to claim 8 as a medicament.

Claim Rejections - "Lack of Enablement"

(10) The Examiner has indicated that the Applicant is not entitled to the full scope of the claims in their present format as the specification as filed is not enabled. In other words, the practitioner would be required to undertake undue experimentation to reproduce the results as reported in the specification for the broad scope of the claimed invention. Indeed, the Examiner has indicated that the specification, in terms of the Examples section beginning at page 32, identifies four constructs only of the human Telomerase RNA Gene Promoter which exhibit promoter activity. Moreover, no further information is said to be provided to enable one of ordinary skill in the art to isolate a promoter sequence and/or fragments thereof differing to the abovementioned four constructs, which display the relevant promoter activity.

However, the Examiner will note that Applicant has amended claim 1 and introduced new independent claim 32 (to the mouse promoter sequence), which introduce further limitations to the scope of the claim as originally filed. In more

detail, claim 1 has been amended and is now limited to a human hTR promoter sequence comprising at least 272 base pairs upstream and at least 69 base pairs downstream of the transcription start site of the hTR gene in question, said promoter sequence being capable of initiating transcription of DNA operably linked downstream of a promoter. Similarly, new claim 32 is limited to the mouse *terc* gene promoter sequence comprising at least 94 base pairs upstream and at least 114 base pairs downstream of the transcription start site of said *terc* gene, said promoter sequence being capable of initiating transcription of DNA operably linked downstream of said promoter. Applicant has thus deleted the phrase "or a fragment thereof" and introduced a a minimal size of promoter, defined by a region spanning an upstream and downstream site of the transcription start site of either said hTR gene or *terc* gene, which can still initiate transcription of DNA. This limitation, therefore, describes that said promoter sequence, in order to initiate transcription, must comprise at least 272 base pairs upstream and 69 base pairs downstream of the transcription start site of the transcription start site of said hTR or 94 base pairs and 114 base pairs of the transcription start site of said *terc* gene, respectively. Applicant has therefore introduced a length limitation in the claimed isolated promoter, which is supported on page 45–46 of the application as filed and Figures 4a and 4b of the application as filed.

Furthermore, in terms of the language in claim 4 directed to mutant, allele, derivative or variants thereof of said abovementioned isolated promoter sequences, the Examiner will note that Applicant has amended original claim 4 and added new claim 33 in order to improve the clarity of said claims. Support for these amendments may be found on, page 7, lines 18–122 and page 9, paragraph 1.

Overall, although the Examiner has indicated that Applicant has only provided exemplification for four constructs of the human telomerase gene promoter in the detailed description and Examples beginning at page 32, Applicant respectfully submits to the Examiner that one skilled in the art would be able to reproduce any of the promoter sequences within the scope of newly amended claim 1 or new claim 28 in view of the sequences presented in Figures 4a and 4b, the restriction enzyme map of the genomic clones as shown in Figure 3a and b, methods presented from page 34 of the application as filed, and/or utilizing molecular biological methods as known to

one skilled in the art. The introduction or deletion of specific base pairs in said isolated promoter sequence, as claimed in claims 4 and 31, as presented, again would be achievable without undue experimentation by one skilled in the art using techniques well known in this field. In view of the limitations in claim 4 and claim 8 the promoter sequence comprising such additional/deleted nucleotides, for example, would obviously still allow transcription of DNA operably linked downstream of said promoters and which would be easily tested using, for example, the luciferase assays as provided on page 35–37 and 44–46 of the description as filed. Applicant therefore submits to the Examiner that in view of the above, one skilled in the art upon reading the present application would be able to isolate the promoter sequences as claimed without unnecessary and improper extensive and undue experimentation. Therefore, the claims as amended, in view of the specification, are in fact enabled.

Claim Rejections–"Indefiniteness"

(14) (a) The Examiner has objected to the phrase "derived from" in claims 1–10, 26 and 27. The Examiner will note that Applicant has deleted this phrase from the claims. Furthermore, it will be seen from the amended claims that the isolated promoter sequence is a promoter sequence for either the human telomerase RNA (hTR) gene or mouse telomerase RNA (*terc*) gene.

(b) The Examiner has objected to the phrase "fragment thereof" in claims 1–10, 26 and 27. Applicant has deleted this phrase from claim 1 and cancelled claims 26 and 27. In claim 1 and claim 28 Applicant has introduced a range of sequence lengths with a lower limit such that the isolated promoter sequence must contain at least 272 base pairs or 94 base pairs upstream of the transcription start sites and 69 or 114 base pairs downstream of the human or mouse genes, respectively.

(c) The Examiner had objected to the phrase "capable of" in claims 1–10, 26 and 27. The Examiner will note that Applicant has amended the claims by deleting this phrase and introducing the positive language "which initiates" as suggested by the Examiner.

(d) The Examiner indicated that there was no proper antecedent basis for "the transcription start site". Therefore, Applicant has amended this phrase to "A

transcription start site of said hTR/*terc* gene" for each of said human and mouse promoter sequence claims, respectively.

(e) The Examiner notes that reference to nucleotide sequences in Figure 5a does not make sense as Figure 5a depicts a bar graph. Applicant has therefore amended claims 2–4 deleting reference to Figure 5a, which is the nucleotide sequence as shown in Figure 4a. Similarly, for the mouse isolated promoter sequence in new claims 31–33 Applicant has made reference to Figure 4b only and SEQ ID identifier NO: 37, as shown in Figure 4b.

(f) The Examiner has objected to the phrase "mutant, allele, derivative or variant thereof" because the definition at pages 8 and 9 of the application as filed is ambiguous. As indicated previously, Applicant has amended claim 4 and introduced language into new claim 31 to more clearly define the relationship of the sequences as claimed with regards to the claimed isolated promoter sequences of claims 1 and new claim 28. Support for these amendments may be found on page 7, lines 18–22 and page 9, lines 1–14.

Applicant believes that in view of our abovementioned comments and amendments to the claims that Applicant has overcome the Examiner's objections to the claims in terms of indefiniteness.

Claim Rejections–"Novelty"

(16) The Examiner has indicated that claims 1, 4–6, 8–10, 26 and 27 are anticipated by cited prior art document Villeponteau et al. (US 5,583,016). The Examiner argues in his summary of this piece of prior art that Villeponteau et al. discloses genomic sequence incorporating sequence upstream of the transcription start site of the human telomerase RNA gene. Indeed, on column 11, paragraph 1 and in view of SEQ ID NO: 3, Villeponteau et al. identify transcription control elements upstream of the transcription start site, such as a A/T box consensus sequence.

However, other than the postulated transcription control elements identified above, Villeponteau et al. do not in fact characterize by evidence the promoter region of the human telomerase RNA gene nor disclose or even suggest the mouse telomerase RNA gene. Thus, although Villeponteau et al. disclose DNA sequence within which such promoter sequences lie, they do not identify regulatory (promoter)

sequences. The promoter sequences of the present invention have been identified by rigorous functional analysis leading to the identification of a minimal promoter sequence, which may initiate transcription of DNA operably linked downstream of said promoter. Indeed, further to the minimal sequence identified upstream of the transcription start site required for promoter activity, the present invention has also identified the inclusion of sequence **downstream** of the transcription start site of the mouse and human genes is desirable for promoter activity. The Examiner will note that independent claim 1 has been amended and new claim 32 has been written to take account of this fact.

Furthermore, Villeponteau et al. do not show functional promoter activity or the use of the promoter sequences of the present invention for the preparation of a medicament for the treatment of cancer, for example. Thus, in view of the amendments to claim 1 and new claim 5 and dependent claims thereof and in view of our abovementioned comments, Applicant respectfully submits to the Examiner that the present invention is indeed novel over Villeponteau et al.

(18) The Examiner has rejected claims 1–6, 8–10, 26 and 27 as being anticipated by Zhao et al. (Oncogene, vol. 16, pages 1345–1350, March 1998). As the Examiner may appreciate, Zhao et al. is the publication which was derived from the priority application (GB 9801902.9, filed 29 January 1998). However, Applicant respectfully submits to the Examiner that this document should not be cited under 35 USC 102 (a) as it was published in March 1998 after the priority date of the corresponding International Application No. PCT/GB99/00308. In view of the enclosed Certified Copy of United Kingdom Application No. 9801902.9, and our comments in response to paragraph 3 of the USPTO Office Communication, Applicant respectfully submits to the Examiner that the present application has a valid claim to priority of the date 29 January 1998 and therefore, Zhao et al. should not be citable as prior art.

Further Amendments

Further to our abovementioned comments, Applicant has identified some obvious errors in Figure 4b as filed and in view of said errors Applicant provides herewith a corrected Figure 4b for the Examiner's attention. In more detail, the

numbers shown to the left of Figure 4b, which should refer to the number of bases upstream of the transcriptional start site, are wrong. Indeed, when related to the arrow indicating the transcriptional start site, the first number to the left of the Figure should read -14 and not -31, -64 and not -81 and so on. Applicant apologizes to the Examiner for any confusion that this obvious error may have caused.

CONCLUSION

Applicant now believes that the pending rejections have been adequately addressed and that the claims as presented are in condition for allowance. The Examiner is encouraged to contact the undersigned directly if such contact will expedite the examination and the allowance of the pending claims.

Respectfully submitted,

Kenneth D. Sibley
Registration No. 31,665

Correspondence Address:

20792
PATENT TRADEMARK OFFICE

CERTIFICATE OF EXPRESS MAILING

"Express Mail" mailing label number: EV353610090US
Date of Deposit: July 14, 2003
I hereby certify that this paper or fee is being deposited with the United States Postal Service "Express Mail Post Office to Addressee" service under 37 CFR 1.10 on the date indicated above and is addressed to Commissioner for Patents, Post Office Box 1450, Alexandria, Virginia 22313-1450.

Vickie Diane Prior